G protein coupled-receptors (GPCRs) have been proven to be the most successful class of drugable targets in the human genome and remain the most attractive family of targets in the modern medicinal chemistry. Recent achievements of structural biology in GPCR research, including growing number of protein structures data, have opened new horizons in this area. Meanwhile accessible qualified chemistry support (*e.g.* high quality hit finding libraries, availability of advanced building blocks for scaffold hopping, efficient hit follow-up and hit-to-lead MedChem optimization) continue to play an important role for rapid and successful project performance.

Being the leading chemical supplier Enamine provides versatile opportunities for GPCR-based Drug Discovery encompassing Design of specific targeted Libraries, diverse off-the-shelf Scaffolds and Building Blocks as well as multiform Custom Chemistry Service.

General GPCR library

27,000 compounds deliverable as entire set or cherry picked subsets

Enamine screening collection of over 2 M diverse small molecular is an excellent source for rapid hit finding in search for new GPCR ligands. A combined approach, including framework 2D-fingerprint similarity search, careful selection of GPCR privileged scaffolds and common moieties with extension of 3D pharmacophore searches, was used to design our General GPCRs targeted Library resulting in a unique set of 27,000 high quality small molecules. All compounds have attractive drug-like structural features and physicochemical profile with appropriative chemical novelty values. The following PhysChem restrictions have been used in construction of the Library:
MW = 250...500, ClogP: = 2…4, TPSA < 150 Å^2, RotBonds ≤ 8, HBD/HBA < 4 / 10
MedChem rules and constraint including PAINS filters have been applied

The main emphasis in the library design was made on ***new Chemotypes and new Molecular Frameworks***

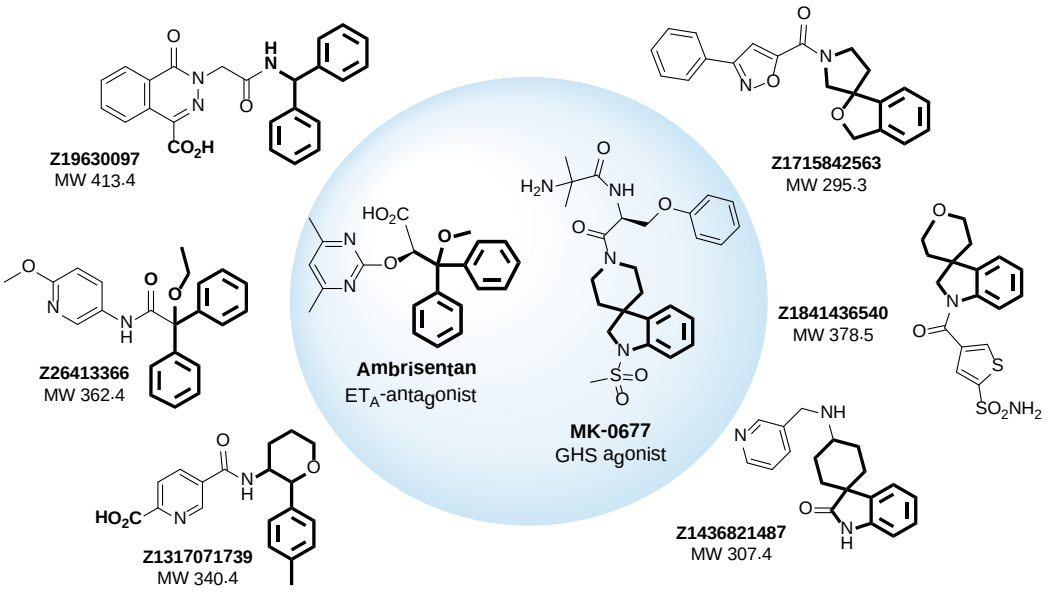
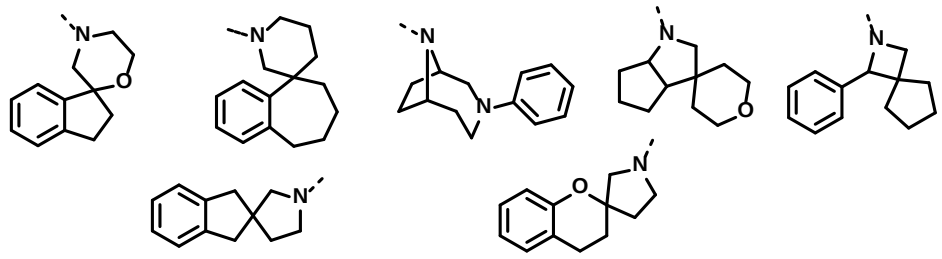


Fig. 1. Examples of Enamine GPCR library compounds having pharmacophore similarity to Ambrisentan (left) and bearing scaffolds that are bioisosteric to the spiro-piperidine-indane privileged fragment (right).



Novel *sp*^{3}-enriched scaffolds specifically designed and synthesized as promising core for new GPCR ligands